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3M

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May 20, 2003

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RE: TSCA 8(E) SUBSTANTIAL RISK NOTICE ON: Phosphonium,
triphenyl(phenylmethyl)-, salt with 1,1,2,2,3,3,4,4,4-nonafluoro-N-methyl-1-
butanesulfonamide (1:1) (CAS 332350-93-3)

Dear Sir:

3M has received data for an acute eye irritation study in rabbits conducted with phosphonium, triphenyl(phenylmethyl)-, salt with 1,1,2,2,3,3,4,4,4-nonafluoro-N-methyl-1-butanesulfonamide (1:1) (CAS 332350-93-3) (TPBP C4 amide) indicating ocular corrosion of the eyelids and nictating membrane.

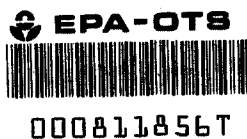
The study was conducted by NOTOX Safety and Environmental Research. Single samples of approximately 51 mg (a volume of approximately 0.1 ml) TPBP C4 amide were instilled into one eye each of three rabbits. Observations were made at 1, 24, 48, and 72 hours after instillation.

Necrosis of the nictating membrane was observed in one animal on days 3 and 4 and in two animals on days 2, 3, and 4. In addition, necrosis of the eyelids was seen in one animal on days 3 and 4. Based on presence of necrosis of the eyelids and/or nictating membrane, it was concluded that ocular corrosion had occurred.

During the observation period, other ocular effects were also noted. Specifically, corneal injury was seen as opacity (maximum grade 2) and epithelial damage (maximum 65% of the corneal area); iridial irritation (grade 1) was observed; and irritation of the conjunctivae was seen as redness, chemosis, and discharge.

A copy of the final report is enclosed.

Please contact Andrew Seacat (651-575-3161) if you have any questions or if we can provide additional information.



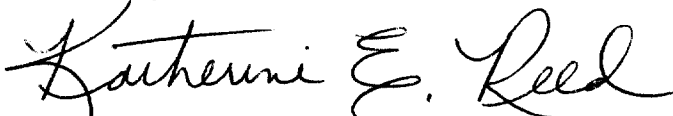
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Page No. 2
May 20, 2003

Once a docket number has been assigned for this submittal, please send the docket number postal card to Cheri Kedrowski, 3M Center Bldg. 220-2E-02, St. Paul, MN 55144.

Sincerely,

A handwritten signature in cursive script that reads "Katherine E. Reed". The signature is written in dark ink and is positioned above the printed name and title.

Katherine E. Reed
Staff Vice President
Environmental Technology and Safety Services

Enclosure

AR 226 - 1323

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REPORT

ACUTE EYE IRRITATION/CORROSION STUDY WITH T-7809 IN THE RABBIT

NOTOX Project 365333
NOTOX Substance 123723

- Page 1 of 10 -

STATEMENT OF GLP COMPLIANCE

NOTOX B.V., 's-Hertogenbosch, The Netherlands

The study described in this report has been correctly reported and was conducted in compliance with the most recent edition of:

The OECD Principles of Good Laboratory Practice which are essentially in conformity with:

United States Environmental Protection Agency (FIFRA). Title 40 Code of Federal Regulations Part 160.

United States Environmental Protection Agency (TSCA). Title 40 Code of Federal Regulations Part 792.

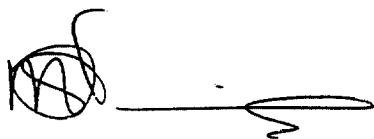
United States Food and Drug Administration. Title 21 Code of Federal Regulations Part 58.

Japanese Ministry of Agriculture, Forestry and Fisheries. 59 NohSan, Notifications No. 3850.

Japanese Ministry of Economy, Trade and Industry. Kanpogyo No. 39 Environmental Agency, Kikyoku No. 85.

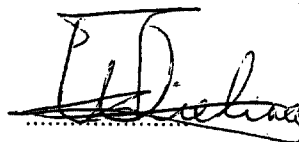
Japanese Ministry of Health, Labor and Welfare. Ordinance No.21.

Study Director:
Drs. M.S. Teunissen



.....
Date: 06 May 2003

Management:
W.J.A.M. Frieling DVM



.....
Date: 6 May 2003

QUALITY ASSURANCE STATEMENT

NOTOX B.V., 's-Hertogenbosch, The Netherlands

This report was audited by the NOTOX Quality Assurance Unit to ensure that the methods and results accurately reflect the raw data.

The dates of Quality Assurance inspections and audits are given below.
During the on-site inspections procedures applicable to this type of study were inspected.

DATES OF QAU INSPECTIONS/ AUDITS	REPORTING DATES
on-site inspection(s)	
11 – 14 November 2002 (Process)	14 November 2002 (SPF Animal Unit)
protocol inspection(s)	
23 December 2002 (Study)	23 December 2002
report audit(s)	
15 April 2003 (Study)	15 April 2003

Head of Quality Assurance:

C.J. Mitchell B.Sc.



Date: 7-5-03

SUMMARY

Acute eye irritation/corrosion study with T-7809 in the rabbit.

The study was carried out based on the guidelines described in: EC Commission Directive 92/69/EEC, B.5, "Acute Toxicity - Eye irritation", OECD No.405, "Acute Eye Irritation/Corrosion" and US EPA, OPPTS 870.2400, Acute Eye Irritation, EPA 712-C-98-195, August 1998.

Single samples of approximately 51 mg of T-7809 (a volume of approximately 0.1 ml) were instilled into one eye of each of three rabbits. Observations were made 1, 24, 48 and 72 hours after instillation.

Instillation of the test substance resulted in effects on the cornea, iris and conjunctivae. Corneal injury was seen as opacity (maximum grade 2) and epithelial damage (maximum 65% of the corneal area) during the observation period.

Iridial irritation (grade 1) was observed during the observation period.

Irritation of the conjunctivae was seen as redness, chemosis and discharge during the observation period.

Necrosis of the nictating membrane was observed in one animal on days 3 and 4 and in two animals on days 2, 3 and 4. In addition, necrosis of the eyelids was seen in one animal on days 3 and 4.

Since sufficient data were available, the study was terminated after 4 days for ethical reasons

Based on the presence of necrosis of the eyelids and/or nictating membranes, it was concluded that ocular corrosion had occurred by instillation of T-7809 into the rabbit eye in all three animals.

Based on these results and according to the EC criteria for classification and labelling requirements for dangerous substances and preparations (Council Directive 67/548/EEC), T-7809 should be labelled as: risk of serious damage to eyes (R 41).

PREFACE

Sponsor	3M Belgium N.V. Haven 1005 Canadastraat 11 B-2070 ZWIJNDRECHT Belgium
Study Monitor	Dr. A Seacat 3 M Medical department 3M Center, Building 220-2E-02 I-94 and Mc
Testing Facility	NOTOX B.V. Hambakenwetering 7 5231 DD 's-Hertogenbosch The Netherlands
Study Director	Drs. M.S. Teunissen
Study Plan	Start: 20 January 2003 End : 23 January 2003

TEST SUBSTANCE

The sponsor is responsible for all test substance data unless determined by NOTOX.

Identification	T-7809
CAS Number	332350-93-3
Description	White crystals
Batch	#1
Purity	See Certificate of Analysis
Test substance storage	At room temperature in the dark
Stability under storage conditions	Stable
Expiry date	01 June 2003
Specific Gravity	1.23

TEST SUBSTANCE PREPARATION

The test substance was ground to a powder using a mortar and pestle prior to weighing.

PURPOSE AND RATIONALE

The purpose of this acute eye irritation/corrosion study was to assess the possible irritation or corrosion potential when a single dose of the test substance was placed in the conjunctival sac of the rabbit eye.

This study should provide a rational basis for risk assessment in man.

The absence of eye pigmentation in the albino rabbit facilitates the evaluation of induced eye reactions. The ocular route was selected because the test substance may accidentally come into contact with the eyes during manufacture, handling and/or use.

GUIDELINES

As required by the Dutch Act on Animal Experimentation, the study protocol was reviewed and agreed by the Article 14-functionary and the Ethical Committee of NOTOX (DEC NOTOX 97-03-10) as required by the Dutch Act on Animal Experimentation (February 1997). The study procedures described in this report were based on the following guidelines:

European Community (EC), Council Directive 67/548/EEC, Annex V, Part B, Methods for the Determination of Toxicity, as last amended by Commission Directive 92/69/EEC, B.5: "Acute Toxicity - Eye Irritation". Official Journal of the European Communities No. L 383, 1992

Organisation for Economic Co-operation and Development (OECD), OECD Guidelines for Testing of Chemicals, Section 4, Health Effects, No.405, "Acute Eye Irritation / Corrosion", Paris Cedex, 1987.

United States Environmental Protection Agency (EPA). Health Effects Test Guidelines, OPPTS 870.2400, Acute Eye Irritation. Office of Prevention, Pesticides and Toxic Substances (7101), EPA 712-C-98-195, August 1998.

ARCHIVING

NOTOX B.V. will archive for at least 10 years raw data, protocol, report and test substance reference sample. No data will be withdrawn without the sponsor's written consent.

TEST SYSTEM

Species	Albino Rabbit, New Zealand White, (SPF-Quality) Recognised by international guidelines as the recommended test system (e.g. EC, OECD) Source: Charles River Deutschland, Kisslegg, Germany
Number of animals	3 Animals of one sex.
Age and body weight	Animals used within the study were at least 6 weeks old and body weights were at least 1.0 kg.
Identification	Earmark.

ANIMAL HUSBANDRY

Conditions

A controlled environment was maintained in the room with optimal conditions considered as being approximately 15 air changes per hour, a temperature of $21 \pm 3^\circ\text{C}$, a relative humidity of 30-70% and 12 hours artificial fluorescent light and 12 hours dark per day.

Deviations from the maximum level for relative humidity (with a maximum of 20%) occurred which might have been caused by cleaning procedures in the room. Based on laboratory historical data these deviations were considered not to have affected the study integrity.

Accommodation

Individually in labelled cages with perforated floors (Scanbur, Denmark, dimensions 56x44x37.5 cm). Acclimatisation period was at least 5 days before start of treatment under laboratory conditions.

Diet

Standard laboratory rabbit diet (Charles River Breeding and Maintenance Diet for Rabbits, Altromin, Lage, Germany) approx. 100 g. per day. Certificates of analysis were examined and retained in the NOTOX archives. In addition, pressed hay (BMI, Helmond, the Netherlands) was provided twice a week.

Water

Free access to tap-water. Certificates of quarterly analysis were examined and retained in the NOTOX archives.

TREATMENT

A health inspection was performed prior to commencement of treatment, to ensure that the animals were in a good state of health. Special attention was paid to the eyes, which were free from any abnormality.

Based on the results of the skin irritation study (no irritation noted), the study was started with three animals. Each animal was treated by instillation of 51.3 mg (50.5 – 52.2 mg) of the test substance (a volume of approximately 0.1 ml) in the conjunctival sac of one of the eyes after gently pulling the lower lid away from the eyeball. The lids were then gently held together for about one second to prevent loss of the test substance. The other eye remained untreated and served as the reference control.

Immediately after the 24-hour observation, a solution of 2% fluorescein in water (adjusted to pH 7.0) was instilled into both eyes of each animal to quantitatively determine corneal epithelial damage. When considered necessary, this procedure was repeated to assess recovery. Any bright green stained area, indicating epithelial damage, was estimated as a percentage of the total corneal area.

OBSERVATIONS

Mortality/Viability	Twice daily.
Toxicity	At least once daily.
Body Weight	Day of treatment (prior to instillation) and at termination.
Necropsy	No necropsy was performed on animals sacrificed for severe irritation/corrosion of the eye.
Irritation	The eyes of each animal were examined approximately 1, 24, 48 and 72 hours after instillation of the test substance. The irritation scores and a description of all other (local) effects were recorded.

The irritation was assessed according to the following numerical scoring system. At each observation, the highest scores given were recorded:

CORNEAL IRRITATION

Opacity: degree of density (area most dense taken for reading)	
No ulceration or opacity (may include slight dulling of normal lustre)	0
Scattered or diffuse areas of opacity, details of iris clearly visible	1
Easily discernible translucent area, details of iris slightly obscured	2
Nacreous area, no details of iris visible, size of pupil barely discernible	3
Opaque cornea, iris not discernible through the opacity	4

Area of cornea involved:	
No ulceration or opacity	0
One quarter or less but not zero	1
Greater than one quarter, but less than half	2
Greater than half, but less than three quarters	3
Greater than three quarters, up to whole area	4

IRIS

Normal	0
Markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperaemia, or injection, any of these or combination thereof, iris still reacting to light (sluggish reaction is positive)	1
No reaction to light, hemorrhage, gross destruction (any or all of these)	2

CONJUNCTIVAL IRRITATION

Redness (refers to palpebrae and sclera, excluding cornea and iris):	
Blood vessels normal	0
Some blood vessels definitely hyperaemic (injected)	1
Diffuse, crimson color, individual vessels not easily discernible	2
Diffuse beefy red	3

Chemosis (refers to lids and/or nictitating membranes):

No swelling	0
Any swelling above normal (includes nictitating membranes)	1
Obvious swelling with partial eversion of lids	2
Swelling with lids about half closed	3
Swelling with lids more than half closed	4

Discharge:

No discharge (may include small amounts observed in inner canthus of normal animals)	0
Any amount different from normal and/or lacrimation	1
Discharge with moistening of the lids and hairs just adjacent to lids	2
Discharge with moistening of the lids and hairs (considerable area around the eye)	3

Where standard lighting was considered inadequate for observing minor effects, eye examinations were performed using an ophthalmic examination lamp.

In cases of equivocal results when comparing the treated and untreated eyes, the illustrated guide from the Consumer Product Safety Commission, Washington, D.C. 20207 was used for additional control purposes.

INTERPRETATION

The results were evaluated according to the EC criteria for classification and labeling of dangerous substances and preparations (Council Directive 67/548/EEC and all adaptations to technical progress and amendments of this Directive published in the Official Journal of the European Communities).

PROTOCOL DEVIATIONS

Deviations from the minimum level of temperature occurred (with a maximum of 1°C). Based on historical laboratory data this deviation was considered not to have affected the study integrity.

RESULTS

Irritation and corrosion (Table 1)

Instillation of approximately 51 mg of the test substance (a volume of approximately 0.1 ml) into one eye of each of three rabbits resulted in effects on the cornea, iris and conjunctivae.

Corneal injury was seen as opacity (maximum grade 2) and epithelial damage (maximum 65% of the corneal area) during the observation period.

Iridial irritation (grade 1) was observed during the observation period.

Irritation of the conjunctivae was seen as redness, chemosis and discharge during the observation period.

Necrosis of the nictating membrane was observed in one animal on days 3 and 4 and in two animals on days 2, 3 and 4. In addition, necrosis of the eyelids was seen in one animal on days 3 and 4.

Since sufficient data were available, the study was terminated after 4 days for ethical reasons

Colouration / Remnants

No staining of (peri) ocular tissues by the test substance was observed.

Toxicity / Mortality

No symptoms of systemic toxicity were observed in the animals during the test period and no mortality occurred.

CONCLUSION

Based on the presence of necrosis of the eyelids and/or nictating membranes, it was concluded that ocular corrosion had occurred by instillation of T-7809 into the rabbit eye in all three animals.

Based on these results and according to the EC criteria for classification and labelling requirements for dangerous substances and preparations (Council Directive 67/548/EEC), T-7809 should be labelled as: risk of serious damage to eyes (R 41).

TABLE 1: INDIVIDUAL EYE IRRITATION SCORES

Time after dosing	Cornea			Iris	Conjunctivae			Comments
	Opacity	Area	Fluor area (%)		Redness	Chemosis	Discharge	
♂ No 89#								
1 hour	1	2		1	2	4	2	-
24 hours	2	3	65	1	3	4	2	-
48 hours	2	3		1	3	4	2	B
72 hours	2	3	55	1	3	4	2	B
♂ No 90#								
1 hour	1	2		1	3	4	2	-
24 hours	2	3	65	1	3	4	2	B
48 hours	2	3		1	3	4	2	AB
72 hours	2	3	55	1	3	4	2	AB
♂ No 91#								
1 hour	1	2		1	2	4	2	-
24 hours	2	2	50	1	3	4	2	B
48 hours	2	1		1	3	4	2	B
72 hours	2	1	25	1	3	3	2	BF

Fluor area (%): green staining (percentage of total corneal area) after fluorescein treatment.

Comments:

- A Grey/white discolouration of the eyelids (sign of necrosis)
 B Grey/white discolouration of the nictitating membrane (sign of necrosis)
 F Reduced elasticity of the eyelids.

TABLE 2: MEAN VALUE EYE IRRITATION SCORES

Animal #	Mean 24 – 72 hours			
	Corneal opacity	Iris	Conjunctivae Redness	Chemosis
89	2	1	3	4.0
90	2	1	3	4.0
91	2	1	3	3.7

Animal specifications:

Animal no	Sex	Age at start (weeks)	Body weights (grams)	
			prior to application	at termination
89	♂	11-13	2537	2582
90	♂	11-13	2348	2341
91	♂	11-13	2376	2470